

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
24 July 2003 (24.07.2003)

PCT

(10) International Publication Number
WO 03/059881 A3

- (51) International Patent Classification⁷: **C07D 207/34**, 417/14, 417/12, 403/14, 409/14, A61K 31/40, 31/427, 31/404, 31/4025, A61P 31/00
- (74) Agent: **MCNEENEY, Stephen, P.**; Eric Potter Clarkson, Park View House, 58 The Ropewalk, Nottingham NG1 5DD (GB).
- (21) International Application Number: PCT/GB02/05916
- (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (22) International Filing Date:
24 December 2002 (24.12.2002)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
0130868.3 24 December 2001 (24.12.2001) GB
- (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- (71) Applicant (*for all designated States except US*): **UNIVERSITY OF STRATHCLYDE** [GB/GB]; 16 Richmond Street, Glasgow G1 1XQ (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (*for US only*): **KHALAF, Abedawn** [GB/GB]; Department of Pure and Applied Chemistry, 295 Cathedral Street, Thomas Graham Building, University of Strathclyde, Glasgow G1 1XL (GB). **WAIGH, Roger** [GB/GB]; Department of Pharmaceutical Sciences, University of Strathclyde, 27 Taylor Street, Glasgow G4 0NR (GB). **SUCKLING, Colin** [GB/GB]; Department of Pure and Applied Chemistry, 295 Cathedral Street, Thomas Graham Building, University of Strathclyde, Glasgow G1 1XL (GB).
- Published:**
- *with international search report*
 - *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*
- (88) Date of publication of the international search report:
27 November 2003
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: DNA MINOR GROOVE BINDING COMPOUNDS

(57) Abstract: There is provided an oligopeptide compound comprising: (a) at least one nitrogen-containing basic group attached to at least one end of the oligopeptide; and (b) two or more heterocyclic monomers, at least one of which is substituted in the heterocyclic part by a branched, cyclic or part cyclic C₃₋₅ alkyl group, or a pharmaceutically acceptable salt or solvate thereof; which compound, salt or solvate binds to the minor groove of DNA.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D207/34 C07D417/14 C07D417/12 C07D403/14 C07D409/14
 A61K31/40 A61K31/427 A61K31/404 A61K31/4025 A61P31/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 698 674 A (HE GONG-XIN ET AL) 16 December 1997 (1997-12-16) cited in the application claims 1-3; figure 15 column 10, line 37 - column 11, line 7 column 16, line 34 - line 59 ---	1-49
Y	US 5 753 629 A (BARALDI PIER GIOVANNI ET AL) 19 May 1998 (1998-05-19) cited in the application abstract; claims 1,3,7-12 ---	1-49
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☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
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- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search

24 September 2003

Date of mailing of the international search report

09/10/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Hass, C

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 Internaⁿ Publication No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	K. EKAMBARESWARA RAO ET AL: "Synthesis of Novel Thiazole-Containing Minor Groove Binding Oligopeptides Related to the Antibiotic Distamycin" J. ORG. CHEM., vol. 55, no. 2, 1990, pages 728-737, XP002255609 Scheme I	1,2,16, 21,25
A	WO 98 21202 A (BARALDI PIER GIOVANNI; CALDARELLI MARINA (IT); BERIA ITALO (IT)) 22 May 1998 (1998-05-22) cited in the application claims 1,4,10	1,2,16, 21,33, 48,49
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A	US 5 273 991 A (LEE MOSES N F) 28 December 1993 (1993-12-28) cited in the application claims 1,41	1,2,16, 21,33
A	US 6 090 947 A (BAIRD ELDON ET AL) 18 July 2000 (2000-07-18) cited in the application figures 2A,2B,3A,3B	1,2,16, 21
A	US 5 637 621 A (BOLONICK JOEL ET AL) 10 June 1997 (1997-06-10) cited in the application column 3, line 43 - line 62	1,2,16, 21
A	EP 0 343 893 A (PFIZER) 29 November 1989 (1989-11-29) page 16, compounds wherein R2 is i-C3H7; page 18, compounds wherein R2 is i-C3H7	1,2,16, 25
A	DWYER T J ET AL: "DESIGN AND BINDING OF A DISTAMYCIN A ANALOG TO D(CGCAAGTTGGC).D(GCCAAGTTGCG): SYNTHESIS, NMR STUDIES, AND IMPLICATIONS FOR THE DESIGN OF SEQUENCE-SPECIFIC MINOR GROOVE BINDING OLIGOPEPTIDES" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, AMERICAN CHEMICAL SOCIETY, WASHINGTON, DC, US, vol. 114, no. 15, 15 July 1992 (1992-07-15), pages 5911-5919, XP000565675 ISSN: 0002-7863 page 5919, left-hand column	1,2,16, 21
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Internationa Application No

PCT/2/05916

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 02 00650 A (GENELABS TECH INC; KHORLIN ALEXANDER (US); MUCHOWSKI JOSEPH MARTIN) 3 January 2002 (2002-01-03) cited in the application page 2, line 30 -page 3, line 27 page 4, line 14 - line 18 page 12, line 11 -page 16, line 25 -----	1,2
X	GUOJIAN XIE ET AL: "Bisindolylmaleimides Linked to DNA Minor Groove Binding Lexitropsins: Synthesis, Inhibitory Activity against Topoisomerase I, and Biological Evaluation" J. MED. CHEM., vol. 39, no. 5, 1996, pages 1049-1055, XP002255610 page 1050, left-hand column, figure 1, compounds 2 and 3 -----	49

INTERNATIONAL SEARCH REPORT

Int

Application No.
PCT/GB 02/05916

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 38-40 and 45-47 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1-15, 29, 31, 32 (all partly)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/SA/ 210

Continuation of Box I.2

Claims Nos.: 1-15, 29, 31, 32 (all partly)

Present claims 1-15 relate to an extremely large number of possible compounds. The number of compounds claimed is extremely large inter alia since only some structural parts of the compounds are given in claims 1 and 2 (and even in dependent claims 3 to 15); moreover, the wording "comprising" does not exclude still other structural features. Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds of claim 16 and the concrete examples given in the description.

Present claims 1, 2, 12, 13, 14, 29, 31 and 32 relate to compounds defined by reference to a desirable characteristic or property, namely:

Claims 1 and 2: The compound shall bind to the minor groove of DNA.

Claim 12: The compound shall be bioavailable.

Claim 13: The compound shall have a high affinity for DNA sequences.

Claim 14: The compound shall bind to the minor groove of a DNA oligomer or polymer with a dissociation constant of less than a certain value.

Claim 29: The compound shall have a specificity for DNA sequences that contain at least one GC base pairing.

Claim 31: The compound shall have different binding activities at different minor groove binding sites in double-stranded DNA molecules having having more than one minor groove binding site.

Claim 32: The different minor groove binding sites mentioned in claim 31 shall comprise solely AT base pairs.

Said claims 1, 2, 12, 13, 14, 29, 31 and 32 lack clarity (Article 6 PCT). An attempt is made to define the compounds by reference to a result to be achieved so that it is not clear for which subject-matter protection is actually sought. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear and supported, namely those parts relating to the compounds comprised by claim 16 and the concrete examples disclosed in the description.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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